



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 610

[Docket No. FDA-2018-N-4757]

RIN 0910-AH95

Revocation of the Test for *Mycoplasma*

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is proposing to amend the biologics regulations by removing the specified test for the presence of *Mycoplasma* for live virus vaccines and inactivated virus vaccines produced from in vitro living cell cultures. FDA is proposing this action because the existing test for *Mycoplasma* is restrictive in that it identifies only one test method in detail to be used even though other methods also may be appropriate. More sensitive and specific methods exist and are currently being practiced, and removal of the specific method to test for *Mycoplasma* provides flexibility for accommodating new and evolving technology and capabilities without diminishing public health protections. This action is part of FDA's implementation of Executive Orders 13771 and 13777. Under these Executive orders, FDA is comprehensively reviewing existing regulations to identify opportunities for repeal, replacement, or modification that will result in meaningful burden reduction, while allowing the Agency to achieve our public health mission and fulfill statutory obligations.

DATES: Submit either electronic or written comments on the proposed rule by [INSERT DATE 75 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before [INSERT DATE 75 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of [INSERT DATE 75 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2018-N-4757 for “Revocation of the Test for *Mycoplasma*.” Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will

not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law.

For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Tami Belouin, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

Table of Contents

I. Executive Summary

A. Purpose of the Proposed Rule

B. Summary of the Major Provisions of the Proposed Rule

C. Legal Authority

D. Costs and Benefits

II. Background

A. Introduction

B. Need for Regulation

III. Legal Authority

IV. Description of the Proposed Rule

A. Scope

B. Appropriate Controls Would Remain in Place

V. Proposed Effective Date

VI. Economic Analysis of Impacts

VII. Analysis of Environmental Impact

VIII. Paperwork Reduction Act of 1995

IX. Federalism

X. Consultation and Coordination with Indian Tribal Governments

XI. References

I. Executive Summary

A. Purpose of the Proposed Rule

FDA proposes to remove the regulation requiring a specified test for the presence of *Mycoplasma* for live virus vaccines produced from in vitro living cell cultures and inactivated virus vaccines produced from such living cell cultures because the regulation is restrictive in that it identifies only one test method in detail to be used even though other methods also may be appropriate. More sensitive and specific methods exist and are currently being practiced, and

removal of the required test for *Mycoplasma* provides flexibility for accommodating new and evolving technology and capabilities without diminishing public health protections.

B. Summary of the Major Provisions of the Proposed Rule

The proposed rule removes § 610.30 (21 CFR 610.30), which details the method for *Mycoplasma* testing of samples of the virus harvest pool and control fluid pool of live virus vaccines and inactivated virus vaccines produced from in vitro living cell cultures.

C. Legal Authority

FDA is taking this action under the biological products provisions of the Public Health Service Act (the PHS Act), and the drugs and general administrative provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

D. Costs and Benefits

Because this proposed rule would not impose any additional regulatory burdens, this regulation is not anticipated to result in any compliance costs and the economic impact is expected to be minimal.

II. Background

A. Introduction

On February 24, 2017, Executive Order 13777, “Enforcing the Regulatory Reform Agenda” (<https://www.federalregister.gov/documents/2017/03/01/2017-04107/enforcing-the-regulatory-reform-agenda>, 82 FR 12285; March 1, 2017) was issued. One of the provisions in the Executive order requires Agencies to evaluate existing regulations and make recommendations to the Agency head regarding their repeal, replacement, or modification, consistent with applicable law. As part of this initiative, FDA is proposing to revoke a regulation as specified in this proposed rule.

B. Need for Regulation

It has become increasingly clear that the test for *Mycoplasma* requirements is too restrictive for live virus vaccines and inactivated virus vaccines produced from in vitro living cell cultures because they specify particular methodologies when alternatives may be available that provide the same or greater level of assurance of safety. Modifications to mycoplasma testing described in § 610.30 must meet the requirements of 21 CFR 610.9.

Thus, the Agency believes that the regulation may no longer reflect the current testing procedures as a general matter and that it is more appropriate, flexible, and efficient to identify appropriate testing requirements for particular products in the biologics license application (BLA).

This proposed rule would remove the specified test for the presence of *Mycoplasma* to provide flexibility for accommodating new and evolving technology and capabilities without diminishing public health protections. Removal of this regulation would allow manufacturers of live virus vaccines produced from in vitro living cell cultures and inactivated virus vaccines produced from such living cell cultures to select the most scientifically appropriate *Mycoplasma* testing method to assure the safety, purity, and potency of their vaccines.

These newer technologies can result in higher sensitivity and specificity of *Mycoplasma* detection and could reduce the time required to complete testing for *Mycoplasma*. Removal of this regulation would not remove *Mycoplasma* testing requirements specified in individual BLAs. A manufacturer of a live virus vaccine produced from in vitro living cell cultures and inactivated virus vaccines produced from such living cell cultures would continue to be required to follow the *Mycoplasma* test requirements specified in its BLA, unless the BLA were revised to modify or replace the test through a supplement in accordance with § 601.12(c) (21 CFR

601.12(c)). FDA would review proposed changes to a manufacturer's approved biologics license in the context of that particular application to ensure that any such action is appropriate.

The proposed rule, if finalized, will remove the regulation; however, a manufacturer would continue to be required to test for *Mycoplasma* as specified in its BLA. If finalized, this action will provide regulated industry with flexibility, as appropriate, to employ advances in science and technology as they become available, without diminishing public health protections. As appropriate, the Agency will describe the appropriate tests for particular products in manufacturers' BLAs.

III. Legal Authority

FDA is issuing this proposed rule under the biological products provisions of the PHS Act (42 U.S.C. 216, 262, 263, 263a, and 264) and the drugs and general administrative provisions of the FD&C Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372, 374, and 381). Under these provisions of the PHS Act and the FD&C Act, we have the authority to issue and enforce regulations designed to ensure that biological products are safe, pure, and potent, and prevent the introduction, transmission, and spread of communicable disease.

IV. Description of the Proposed Rule

A. Scope

The test for *Mycoplasma* in § 610.30 is intended to ensure that live virus vaccines produced from in vitro living cell cultures, and inactivated virus vaccines produced from such living cell cultures do not contain *Mycoplasma*. Currently the regulation details the method for *Mycoplasma* testing of samples of the virus harvest pool and control fluid pool of live virus vaccines and inactivated virus vaccines produced from in vitro living cell cultures. Removal of

this regulation would eliminate a restrictive and duplicative requirement and accommodate new and evolving technology.

We are proposing to remove the specified test for the presence of *Mycoplasma* for live virus vaccines produced from in vitro living cell cultures and inactivated virus vaccines produced from such living cell cultures. FDA is proposing this action because the existing specified test for the presence of *Mycoplasma* is restrictive and duplicative of requirements that are also specified in the BLA. This change is intended to remove restrictive or duplicative requirements and accommodate new and evolving technology and capabilities without diminishing public health protections. Removal of this regulation would not remove *Mycoplasma* testing requirements specified in individual BLAs. A biological product manufacturer would continue to be required to follow the *Mycoplasma* testing requirements specified in its BLA unless the BLA were revised to modify or replace the test through a supplement in accordance with § 601.12(c). FDA would review proposed changes to a manufacturer's approved biologics license in the context of that particular license to ensure that any such action is appropriate.

FDA is proposing to remove the requirements contained in § 610.30 from the regulations. As a result of removing § 610.30, we would also remove and reserve 21 CFR part 610, subpart D. FDA is proposing this action because the testing method described in the regulation is restrictive and more sensitive and specific testing methods are now available.

B. Appropriate Controls Would Remain in Place

FDA believes that if this rulemaking becomes finalized as proposed, we would be able to continue to ensure that appropriate controls remain in place. If the proposed rule is finalized and the regulation calling for a specific test for *Mycoplasma* is eliminated, manufacturers would continue to be required to perform a test for *Mycoplasma* described in their BLAs for their

licensed live virus vaccines produced from in vitro living cell cultures and their inactivated virus vaccines produced from such cultures. Such requirement would remain in effect unless the BLA were revised to modify or replace the test through a supplement in accordance with § 601.12(c). FDA would review proposed changes to a manufacturer's approved biologics license in the context of that particular license to ensure that any such action is appropriate.

V. Proposed Effective Date

FDA is proposing that any final rule based on this proposed rule become effective 30 days after the date of its publication in the *Federal Register*.

VI. Economic Analysis of Impacts

We have examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, Executive Order 13771, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Executive Order 13771 requires that the costs associated with significant new regulations "shall, to the extent permitted by law, be offset by the elimination of existing costs associated with at least two prior regulations." We believe that this proposed rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because this proposed rule would increase flexibility and does not add any new regulatory responsibilities, we propose to certify

that the proposed rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$150 million, using the most current (2017) Implicit Price Deflator for the Gross Domestic Product. This proposed rule would not result in an expenditure in any year that meets or exceeds this amount.

We believe industry will largely maintain their current practices following the removal of § 610.30 Test for *Mycoplasma*. Although manufacturers of live virus vaccines and inactivated virus vaccines produced from in vitro living cell cultures may experience some unquantifiable cost savings from streamlining their testing procedures, we predict no quantifiable cost savings. FDA will also maintain its current practices, similarly generating no quantifiable cost savings. Therefore, we expect this proposed rule to be cost neutral.

We have developed a comprehensive Preliminary Economic Analysis of Impacts that assesses the impacts of the proposed rule. The full preliminary analysis of economic impacts is available in the docket for this proposed rule and at <https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm>.

VII. Analysis of Environmental Impact

We have determined under 21 CFR 25.31(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Paperwork Reduction Act of 1995

FDA tentatively concludes that this proposed rule contains no collection of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

IX. Federalism

We have analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. We have determined that this proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we conclude that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

X. Consultation and Coordination with Indian Tribal Governments

We have analyzed this proposed rule in accordance with the principles set forth in Executive Order 13175. We have tentatively determined that the rule does not contain policies that would have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes. The Agency solicits comments from tribal officials on any potential impact on Indian Tribes from this proposed action.

XI. Reference

The following reference is on display at the Dockets Management Staff (see ADDRESSES) and is available for viewing by interested persons between 9 a.m. and 4 p.m. Monday through Friday; it is also available electronically at <https://www.regulations.gov>. FDA has verified the website address, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

1. FDA/Economics Staff, “Elimination of 21 CFR 610.30 Test for *Mycoplasma*, Preliminary Regulatory Impact Analysis, Preliminary Regulatory Flexibility Analysis, Unfunded Mandates Reform Act Analysis,” 2018. (Available at: <https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm>.)

List of Subjects in 21 CFR Part 610

Biologics, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 610 be amended as follows:

PART 610--GENERAL BIOLOGICAL PRODUCTS STANDARDS

1. The authority citation for part 610 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372, 374, 381; 42 U.S.C. 216, 262, 263, 263a, 264.

Subpart D--[Removed and Reserved]

2. Remove and reserve subpart D, consisting of § 610.30.

Dated: March 26, 2018.

Scott Gottlieb,

Commissioner of Food and Drugs.

[FR Doc. 2019-06188 Filed: 4/1/2019 8:45 am; Publication Date: 4/2/2019]